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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,126	08/23/2006	Yehudit Natan	27586U	5429

20529 7590 01/26/2010

THE NATH LAW GROUP
112 South West Street
Alexandria, VA 22314

EXAMINER	
RUSSEL, JEFFREY E	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
01/26/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,126	NATAN ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-63 and 66-93* is/are pending in the application.

4a) Of the above claim(s) *67-91 and 93* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-63,66 and 92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20091009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

1. This application contains claims 73-85 and 93 drawn to an invention nonelected with traverse in the reply filed on April 6, 2009. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 67-72 and 86-91 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on April 6, 2009.

2. The disclosure is objected to because of the following informalities: The claim for priority in the first paragraph of the specification, inserted by the amendment filed October 26, 2009, is objected to because the filing date given for provisional application 60/540,557 is incorrect. The correct filing date for this provisional application is February 2, 2004. Appropriate correction is required.

3. The amendment filed October 26, 2009 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: The amendment inserting the claim for priority as the first paragraph contains new matter because of its incorporation by reference to the content of the two provisional applications. The application as originally filed did not include an incorporation by reference statement, and the insertion of such a statement after the filing date of the application is new matter. See MPEP 201.11(III)(F), last paragraph. Applicant is required to cancel the new matter in the reply to this Office Action.

4. Claim 92 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "essentially free" in claim 92, step (a), is indefinite because the phrase is given two different conflicting definitions in Applicants' specification. See page 12, lines 9-20, and page 16, lines 12-13. It can not be determined which definition of the phrase provided by Applicants is controlling.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. Claims 54-59, 63, and 92 are rejected under 35 U.S.C. 102(b) as being anticipated by Gen (U.S. Patent Application Publication 2002/0119946). Gen teaches adding an aqueous saline solution comprising polyphenols to an aqueous solution of a protein such as insulin, interferon-alpha, EGF, and protein allergens, or to an aqueous solution of DNA, and then freeze-drying the mixture. The polyphenols can be epigallocatechin gallate and can be extracted from green tea. The polyphenol solutions are not described as comprising glycerol, DMSO, or polyalcohols. See, e.g., the Abstract; paragraphs [0009] - [0011]; Examples 1-3, 5, and 6. The solutions of proteins and DNA of Gen correspond to Applicants' biological fluids. The time period which occurs between Gen's freeze-drying step and Gen's subsequent use of the complexes corresponds to Applicants' storing under appropriate storing conditions. Because the polyphenols of Gen are dissolved in aqueous saline solution prior to complexing and freeze-drying, inherently the freeze drying of Gen will occur at a temperature below 0°C, because the presence of solutes depresses the freezing point of a solution below that of the solvent. Sufficient evidence of similarity is deemed to be present between the method of Gen and

Applicants' claimed method to shift the burden to Applicants to provide evidence that the claimed method is unobviously different than that of Gen.

7. Claims 54-56, 58-60, 62, 63, 66, and 92 are rejected under 35 U.S.C. 103(a) as being obvious over Mann et al (U.S. Patent Application Publication 2003/0059338). Mann et al teach combining thrombin in solution form with epicatechin and bovine serum albumin, lyophilizing the mixture, and then subjecting the lyophilized mixture to gamma irradiation for purposes of sterilization. There is no description or indication of glycerol, DMSO, or polyalcohols being combined with the thrombin. See, e.g., the Abstract and paragraph [0098]. The thrombin solution of Mann et al corresponds to Applicants' biological fluid. The bovine serum albumin of Mann et al corresponds to Applicants' macromolecule. During the time after lyophilization, up to and after the gamma irradiation step, the lyophilized mixture of Mann et al inherently is being stored by Mann et al. Note that Applicants' claims do not require any particular storing procedures, storing times, or storing conditions. Mann et al do not teach combining epicatechin and bovine serum albumin in the form of a solution with the thrombin solution. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine epicatechin and bovine serum albumin in the form of a solution with the thrombin solution, because it is easier to mix ingredients in solution form, because the solvent would be removed by the lyophilization step and thus would not be expected to interfere with the final product, and because use of a solvent for the epicatechin and bovine serum albumin would not appear to result in any different properties for the lyophilized mixture. More generally, Mann et al teach sterilization of biological materials including stem cells, red blood cells, white blood cells, and monocytes, in which the biological materials are combined with a flavonoid/flavonol

stabilizer including epigallocatechin gallate and an optional additional stabilizer including trehalose, and wherein the residual solvent content of the biological material is reduced prior to irradiation, such as by lyophilization. The biological materials, including the lyophilized biological materials, are stored under vacuum or in an inert atmosphere prior to irradiation. See, e.g., paragraphs [0027], [0031], [0036], [0037], [0058], [0059], [0078], and [0081]. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to subject the biological materials including stem cells, red blood cells, white blood cells, and monocytes of Mann et al to lyophilization, storage, and irradiation in the presence of stabilizers including epigallocatechin gallate and trehalose because Mann et al teach the desirability of sterilizing such biological materials, and teach the utility of combinations of treatments, i.e. use of a stabilizer, lyophilization, and storage under vacuum prior to irradiation, in order to sterilize the biological materials. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine the stabilizers of Mann et al in the form of a solution with the biological material to be sterilized, because it is easier to mix ingredients in solution form, because the stabilizer solvent would be removed by the lyophilization step and thus would not be expected to interfere with the final product, and because use of a solvent for the stabilizers would not appear to result in any different properties for the lyophilized mixture.

8. Claims 54-61 and 63 are rejected under 35 U.S.C. 103(a) as being obvious over the WO Patent Application 03/099040. The WO Patent Application '040 teaches combining white wine vinasses, maltodextrin, blueberry extract, and green tea extract, and freeze drying the mixture. See Example 2. The white wine vinasses and blueberry extract of the WO Patent Application '040 correspond to Applicants' biological material which can be a biological fluid; and the

maltodextrin of the WO Patent Application '040 corresponds to Applicants' macromolecule. During the time after freeze drying, up until the lyophilized mixture's use as a dietary supplement, the freeze dried mixture of the WO Patent Application '040 inherently is being stored by the WO Patent Application '040. Note that Applicants' claims do not require any particular storing procedures, storing times, or storing conditions. The WO Patent Application '040 does not teach combining maltodextrin and green tea extract in the form of a solution with the white wine vinasses and blueberry extract. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to combine maltodextrin and green tea extract in the form of a solution with the white wine vinasses and blueberry extract, because it is easier to mix ingredients in solution form, because the solvent would be removed by the lyophilization step and thus would not be expected to interfere with the final product, and because use of a solvent for the maltodextrin and green tea extract would not appear to result in any different properties for the freeze dried mixture. The WO Patent Application '040 does not teach a method in which dextran is combined with a wine vinasse and the resulting mixture is freeze dried. However, the WO Patent Application '040 teaches that dextran is a bioavailability promoter which is useful for combining with wine vinasses, and that bioavailability promoters in general can be combined with the wine vinasses prior to freeze-drying. See, e.g., page 3, line 27 - page 4, line 8, and page 5, lines 8-9. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to substitute dextran for maltodextran in Example 2 of the WO Patent Application '040 as modified above, because substitution of one known functional equivalent for another with only the expected retention of function, i.e. bioavailability promotion, is prima facie obvious.

9. Applicant's arguments filed October 26, 2009 have been fully considered but they are not persuasive.

Applicants' arguments appear to make citations to U.S. Patent Application Publication 2007/0178434, which was published based upon the instant application. However, it is the instant application, and not the patent application publication which is being examined. Any citations in Applicants' responses should be directed to the original papers filed in this application rather than to the patent application publication.

The rejection of claim 92 under 35 U.S.C. 112, second paragraph, is maintained. Applicants contend that the two definitions of "essentially free" set forth in the specification apply to two different components, the one on page 12 applying to polyalcohols, and the one on page 16 applying to additives. However, page 16, lines 9-10, defines additives as including polyalcohols. Accordingly, both definitions apply to polyalcohols, and to the extent that the two definitions conflict with one another, it can not be determined which applies to "essentially free" as used in claim 92.

The anticipation rejection based upon Gen (U.S. Patent Application Publication 2002/0119946) is maintained. Applicants contend that the reference does not teach the biological materials specified in amended claim 54, but do not provide any reasons why the reference does not teach "biological fluids" in particular. Applicants' specification does not provide any particular definition for the term "biological fluid", and aqueous solutions comprising biologically derived or biologically active proteins and DNA are deemed to constitute biological fluids.

The obviousness rejection over Mann et al (U.S. Patent Application Publication 2003/0059338) is maintained. Applicants contend that there is no motivation to modify Mann et al in order to arrive at the presently claimed subject matter, and that Mann et al is not enabled for anything more than the freezing of "pertinacious" [sic - proteinaceous?] material. Firstly, it should be noted that Applicants' arguments do not always correctly summarize the currently claimed invention. For example, at page 21, last paragraph, of Applicants' response, the second sentence states "that the presently claimed subject matter is aimed at preservation of cells or cell containing tissues or organs". However, "biological material" has been amended in claim 54 to include biological fluids, natural liposomes, and synthetic liposomes, which are not cell-containing materials. Therefore, Mann et al's disclosure of the formation of lyophilized thrombin compositions at paragraph [0096] continues to be applied against the instant claims.

Secondly, concerning Applicants' contention of lack of motivation to modify Mann et al to arrive at the presently claimed subject matter, it should be noted that the issue of motivation under 35 U.S.C. 103(a) concerns those aspects of a claimed invention which are not taught in a prior art reference. Mann et al's sterilization by irradiation step occurs subsequent to Mann et al's lyophilization. Such a step is not excluded from Applicants' claims, i.e. Applicants' "comprising" language does not set forth any limitations on what can happen to the freeze-dried biological material subsequent to storing step (c). Mann et al's sterilization is not excluded from the scope of Applicants' claims, i.e. is not a difference between the teachings of Mann et al and Applicants' claimed method which needs to be resolved under 35 U.S.C. 103(a). Patentability must be based upon claimed, not unclaimed, differences over the prior art.

Concerning Applicants' contention that Mann et al is non-enabled except for freeze-drying of proteins, it should be noted that references are presumed operable and enabled, and the burden is on Applicants to provide evidence that a reference applied under 35 U.S.C. 102 or 103 is non-enabled. See MPEP 716.07 and 2121. Applicants have provided no evidence that Mann et al is non-enabled with respect to the freeze-drying of, e.g., stem cells, red blood cells, white blood cells, and monocytes. Because actual reduction to practice is not a requirement for patentability, the lack of working examples in the disclosure of Mann et al for the freeze-drying of cells does not constitute evidence of lack of enablement. In any event, Mann et al contains disclosure, e.g., at paragraphs [0063]-[0069], [0080], and [0081], as to how to effect sterilization while protecting the desired biological material which is to be sterilized. Finally, Applicants' summary of Mann et al at page 23, last paragraph, lines 5-6, is inaccurate. Clearly, Mann et al do not aim to reduce or eliminate "any" cellular matter in the material, because this interpretation would render non-sensical Mann et al's inclusion of cells as materials which can be freeze-dried and sterilized (see paragraph [0027]). Mann et al intend to reduce or eliminate biological contaminants or pathogens (see paragraph [0029]), not desired biological materials such as Mann et al's exemplified stem cells, red blood cells, white blood cells, and monocytes.

The Natan et al article (PLoS ONE, Vol. 4, page e5240) attached to Applicants' response has been considered. However, the Natan et al article is not a prior art publication, and the contents of the Natan et al article have not been submitted in affidavit or declaration form under 37 CFR 1.132. Accordingly, the Natan et al article can not be relied upon to overcome the prior art rejection based upon Mann et al. Further, the Natan et al article does not appear to contain any evidence demonstrating any result of Applicants' freeze drying method which does not also

occur in Mann et al's freeze-drying method, e.g., there is no side-by-side comparison that cell viability is preserved in Applicants' claimed freeze drying method but not in Mann et al's disclosed freeze drying method, which also requires the presence of polyphenols. Note that freeze-drying in the presence of polyphenols is not a difference between the method of Mann et al and Applicants' claimed method. Again, while Mann et al require a sterilization step subsequent to their freeze-drying step, a subsequent sterilization step is not excluded from the scope of Applicants' claims, and does not constitute a difference between Applicants' claimed method and Mann et al's disclosed method.

The obviousness rejection based upon the WO Patent Application 03/099040 is maintained. At pages 26-27 of the response, Applicants contend that the WO Patent Application '040's dietary supplement does not include viable cells, and that the WO Patent Application '040's method can not be employed for freeze drying or cryopreserving viable cells. The examiner agrees; however, because the rejected claims do not require the presence of viable cells, these arguments are not convincing. Patentability must be based upon claimed, not unclaimed, differences, over the prior art.

10. The two references crossed off from the Information Disclosure Statement filed October 9, 2009 were not considered because the references are not in English, and a concise explanation of the references' relevance was not provided as required by 37 CFR 1.98(a)(3)(i).

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/
Primary Examiner, Art Unit 1654

JRussel
January 26, 2010